

# An Outbreak of Foxglove Leaf Poisoning

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Comfrey (*Symphytum officinale*) leaves resemble those of foxglove (*Digitalis purpurea*) when the plant is not in bloom and, therefore, cardiac glycoside poisoning may occur when people confuse foxglove with comfrey. We report an outbreak of foxglove leaf poisoning following the use of alleged "comfrey" herbal tea. Nine patients were involved and initially presented with nausea, vomiting, diarrhea and dizziness. Significant cardiotoxicity developed later among the 3 patients who also had mild hyperkalemia. Peak serum digoxin concentration measured by immunoassay was elevated in all patients and ranged from 4.4 ng/mL to 139.5 ng/mL. Patients with severe cardiotoxicity were treated with temporary cardiac pacing. Moreover, 40–80 mg of digoxin-specific antibody therapy was given without any effect. All patients recovered uneventfully. Our report highlights the potential risk of misidentification of herbs; in this case, *D. purpurea* was mistaken for *S. officinale*. Physicians should be aware that cardiac glycoside poisoning could arise from such misidentification. Public education about the toxicity of *D. purpurea* poisoning may reduce the risk of misidentification and subsequent poisoning. [*J Chin Med Assoc* 2010;73(2):97–100]

**Key Words:** acute plant poisoning, cardiac glycoside, comfrey, *Digitalis purpurea*

## Introduction

Foxglove (*Digitalis purpurea*) is native to Europe, northwestern Africa, and western and central Asia. It contains several potent cardiac glycosides and metabolites, namely digitoxin, gitoxin, lanatoside C and digitoxigenin, with digitoxin being the most prominent.<sup>1</sup> There are few clinical reports of confusing comfrey leaves with foxglove leaves. We report an outbreak of *D. purpurea* poisoning from drinking alleged "comfrey" herbal tea.

## Case Reports

### Case 1

The first case was a 62-year-old female with a history of type 2 diabetes mellitus under insulin therapy. She was with her neighbors when she drank several mouthfuls of herbal tea, which she believed to be made from comfrey leaves, for liver protection and reducing

"body heat". The leaves had been picked by one of her neighbors in a national park 1 day earlier. Approximately 4 hours later, our patient experienced nausea, repeated vomiting, numbness of the arms and a headache, and presented to the emergency department (ED) of a district hospital.

On arrival, her vital signs were as follows: heart rate was 88 beats/min and blood pressure was 156/80 mmHg. Physical examinations revealed epigastric tenderness and a regular heart sound with a grade 2/6 systolic murmur. An initial electrocardiogram (ECG) disclosed sinus tachycardia. Other laboratory tests showed mild hyperkalemia (5.1 mmol/L; reference, 3.4–4.7 mmol/L). With a tentative diagnosis of acute gastritis, she was given intravenous metoclopramide and admitted for observation.

### Case 2

The second case was a 60-year-old female with a history of dilated cardiomyopathy, congestive heart failure and atrial fibrillation. She developed vertigo, severe



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vomiting with coffee-ground vomitus, and dyspnea approximately 4 hours after drinking the same herbal tea as Case 1. On presentation to the ED, she was afebrile and hemodynamically stable. An initial ECG disclosed atrial fibrillation with a heart rate of 82 beats/min. Laboratory tests were all within normal limits except for mild hyperkalemia (5.6 mmol/L) and 4+ stool occult blood test. The patient received upper gastrointestinal endoscopy several hours later, which showed esophagitis and superficial gastritis. She was treated with an H<sub>2</sub> antagonist and was admitted for further management.

Although both patients were relatively stable at the beginning of treatment, gastrointestinal symptoms deteriorated and ECG showed atrial flutter and junctional tachycardia after hospitalization. Emergent consultation with a cardiologist was sought, and both patients were transferred to the intensive care unit for cardiac monitoring. Because *D. purpurea* poisoning was suspected, serum digoxin concentrations were measured by employing Synchron digoxin reagent (Beckman Coulter Inc., Brea, CA, USA). These concentrations were 139.7 ng/mL (reference range, 0.8–1.2 ng/mL) for the first patient, and 66.6 ng/mL for the second patient. The herb used to make the tea was later identified as foxglove, rather than comfrey.

At this time, emergency physicians were already alerted to a possible outbreak of cardiac glycoside poisoning. Another 7 patients, who were neighbors of Case 1, subsequently presented to the ED on the same day with gastrointestinal manifestations similar to those of the first 2 patients. All 9 patients received close ECG monitoring and periodic measurements of serum digoxin concentrations.

Although all patients had elevated serum digoxin concentrations (Table 1), the onset and magnitude of toxic manifestations varied widely between patients. The first 3 patients presented with severe cardiotoxicity requiring a temporary cardiac pacemaker, which was unresponsive to 40–80 mg of digoxin-specific antibody (Digibind®) therapy. These patients also had a higher initial potassium concentration and needed longer hospitalization than the other 6 patients, who manifested only mild gastrointestinal symptoms such as nausea, vomiting and epigastralgia. All patients recovered without sequelae.

## Discussion

Foxglove and comfrey flowers are very different and thus they are easily identified (Figure 1). However,

**Table 1.** Clinical data of 9 patients in an outbreak of foxglove leaf poisoning

Case	Age (yr)/sex	Past history	Onset (hr)	Presenting symptoms	Electrocardiographic change	Peak SDC (ng/mL)	Initial K <sup>+</sup> (mmol/L)	Specific interventions	Hospital stay (d)
1	62/F	DM	4	Headache, nausea, numbness, vomiting	Atrial flutter	139.5	5.1	TCP/digibind	8
2	60/F	CAD, DCM	3	Abdominal pain, dizziness, nausea, vomiting	Junctional tachycardia, ventricular premature contractions	66.6	5.6	TCP/atropine/digibind	8
3	65/F	DCM	7	Dizziness, dyspnea, vomiting	Paroxysmal atrial fibrillation	131.7	5.0	TCP/digibind	10
4	62/M	None	6	Dizziness	Premature ventricular contractions	28.8	4.1	–	6
5	60/F	None	3	Diarrhea, nausea, vomiting	Sinus bradycardia	31.1	4.1	Atropine	6
6	68/F	None	N/A	Nausea, vomiting	Sinus pause	55.9	4.0	–	6
7	71/F	None	3	Dizziness, nausea, vomiting	Sinus arrest	41.4	4.5	Atropine	6
8	61/F	CKD	N/A	Diarrhea, nausea, vomiting	Normal sinus rhythm	4.4	4.2	–	7
9	71/F	HCVD, CAD	N/A	Abdominal pain, dizziness, nausea, vomiting	Sinus bradycardia	10.6	4.2	–	3

DM = diabetes mellitus; CAD = coronary artery disease; DCM = dilated cardiomyopathy; CKD = chronic kidney disease; HCVD = hypertensive cardiovascular disease; N/A = relevant information not available; SDC = serum digoxin concentration; TCP = transcutaneous pacemaker.

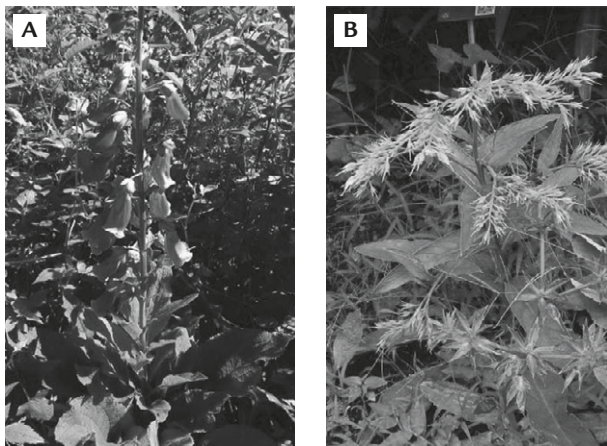
comfrey leaves resemble those of foxglove when the plants are not in bloom (Figure 2). Accidental foxglove poisoning may thus occur when people accidentally collect foxglove instead of comfrey. Surprisingly, there are very few clinical reports of such poisoning in the literature.

Comfrey has been used as a herbal medicine for more than 2,000 years for treating fractures, tendon injury, gastrointestinal tract ulceration, lung congestion, joint inflammation, and promoting wound healing. Regular use of *S. officinale*, however, can result in hepatotoxicity, hepatic veno-occlusive disease, and even cancer due to pyrrolizidine alkaloids.<sup>2</sup> In addition to the potential toxic effect of comfrey, acute poisoning can occur when there is misidentification of foxglove for comfrey. To our knowledge, there are 4 previous clinical reports of confusion between foxglove with comfrey.<sup>3-6</sup> A total of 6 victims were involved, and 2 received digoxin-specific antibody.

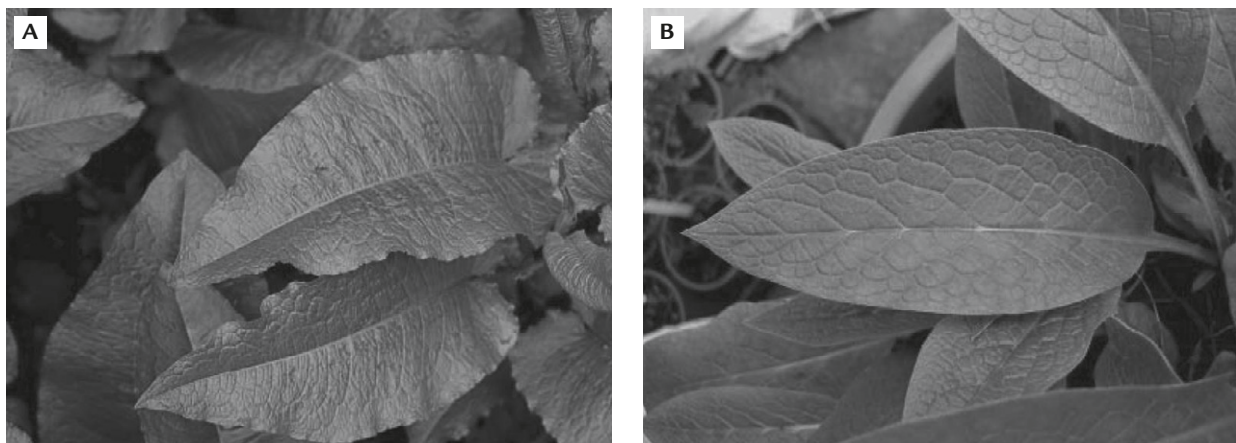
All victims fully recovered. The clinical features of *D. purpurea* poisoning in this outbreak were similar to those of documented cardiac glycoside poisoning, with early gastrointestinal manifestations and later cardiotoxicity and neurotoxicity. Life-threatening effects, such as severe cardiotoxicity or shock, can develop after poisoning; however, only a few fatal *D. purpurea* poisonings have previously been reported.<sup>7</sup> The initial presentations of foxglove poisoning are rather nonspecific and not easily differentiated from those of other food-borne diseases or gastrointestinal problems. Delayed diagnosis can therefore occur, as shown in the first 2 cases. Accurate and timely diagnosis of acute cardiac glycoside poisoning depends on the physician's high index of suspicion and careful history-taking.

Three of our patients had higher serum potassium concentrations and presented with more severe cardiotoxicity. Hyperkalemia is considered as a poor prognostic factor in acute digitoxin poisoning.<sup>8</sup> However, it is uncertain whether this finding is applicable to other patients with cardiac glycoside poisoning since a fatal case reported by Ramlakhan and Fletcher had a potassium concentration of 4.3 mmol/L.<sup>7</sup> Despite inconsistent findings, close monitoring and prompt correction of serum potassium concentrations are probably warranted in the prevention of potential cardiac arrhythmias in cardiac glycoside poisoning.

Various cardiac glycosides are known to cross-react with commercial serum digoxin immunoassays. We found high serum digoxin concentrations with a range of 4.4–139.5 ng/mL in all of our patients. Accurate digitoxin concentrations might be obtained by employing gas chromatography or high-performance liquid chromatography.<sup>9</sup> However, the equipment for these techniques is not commonly available at the ED. While presenting digoxin-like substances as in the case of



**Figure 1.** The flowers of (A) foxglove and (B) comfrey are quite different.



**Figure 2.** The broad leaves of (A) foxglove resemble those of (B) comfrey when the plants are not in bloom.

*D. purpurea* poisoning, serum digoxin concentrations do not provide helpful information on the degree of toxicities and appropriate dosing of digoxin-specific antibody.

Digoxin-specific antibody therapy is recommended for use in cardiac glycoside poisoning with potentially life-threatening arrhythmias (e.g. serious bradycardia, ventricular arrhythmia or asystole) and/or hyperkalemia after standard therapy has failed.<sup>10</sup> Although the efficacy of digoxin-specific antibody remains uncertain in *D. purpurea* poisoning, such a therapy may still be recommended for patients with severe foxglove poisoning. Three of our patients received 40–80 mg of digoxin-specific antibody treatment 2 days post-ingestion because of persistent bradycardia and mild hyperkalemia. While it was debatable whether these 3 patients should have received digoxin-specific antibody therapy, none of them responded to the therapy either because of insufficient dosing or delayed timing of administration. Avoiding irreversible vital organ damage is still the keystone of managing foxglove poisoning.

Herbal teas are commonly consumed in most parts of the world, but potential toxicity of herbs should not be overlooked. Physicians should be aware that patients who use herbal teas could confuse *S. officinale* leaves with *D. purpurea* leaves, resulting in acute cardiac glycoside poisoning. Public education about the toxicity of *D. purpurea* poisoning may reduce the risk of both misidentification and subsequent poisoning.

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